UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ROCHE DIAGNOSTICS GMBH, et al.,

Plaintiffs,

-v-

ENZO BIOCHEM, INC., et al.,

Defendants.

No. 04 Civ. 04046 (RJS)

ROCHE'S RESPONSIVE BRIEF REGARDING
CLAIM CONSTRUCTION OF U.S. PATENT NOS. 4,943,523 AND 5,082,830

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I. INTRODUCTION

Enzo's claim constructions are based on conclusory assertions unsupported by the patent specification, file history, or any extrinsic evidence. Enzo has taken positions that are not only internally inconsistent and contradictory, they are also contrary to its interrogatory responses and its own statements in the intrinsic record. Further, Enzo argues that several disputed claim terms should be given their "plain meaning," even though Roche has presented a material dispute as to what the "plain meaning" is and also proposed a clarifying construction that resolves the dispute. In those instances, Enzo is effectively seeking to have the jury decide the claim construction dispute between the parties, which is impermissible as a matter of law. *See, e.g., O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1361 (Fed. Cir. 2008) ("A determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate when a term has more than one 'ordinary' meaning or when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute.").

With respect to U.S. Patent No. 4,943,523 ("the '523 Patent"), Enzo's primary argument appears to be that "process" limitations cannot be applied to compound claims. That is not the law, particularly in cases where, as here, the patentee describes the claimed invention as being the product of purportedly novel methods. *AFG Indust., Inc. v. Cardinal IG Co*., 224 F. App'x 956, 958-59 (Fed. Cir. 2007) ("[T]he process by which a product is produced can limit a product claim when, as here, the process is relied on for patentability and validity"); *In re Fenofibrate Patent Litig.*, No. 11 MDL 2241, 2011 WL 10901800, *2 (S.D.N.Y. Aug. 23, 2011), *aff'd*, 499 Fed. App'x 974 (Fed. Cir. 2013) (product claim can be limited by the method of manufacture where the specification sets forth a limitation as defining "'the present invention,' a phrase that the Federal Circuit has repeatedly construed as indicative of a definitional limitation on the claim term itself.") (citations omitted). The claimed compounds are properly interpreted by reference to the chemical reactions which led to those compounds not only because the '523 Patent defines the invention as methods of preparing labeled molecules and the products of such methods, *see* '523 Patent, 3:24-30, 1:10-13 ("[t]he invention . . . relates to the products obtained from these

methods"), but also because Enzo repeatedly described and explained the claimed invention to the Patent Office by reference to those chemical reactions.

II. THE '523 PATENT

A. CONSTRUCTION OF DISPUTED CLAIM TERMS

1. "reactive group"

The primary dispute is whether this claim term should be construed to account for the chemical function of the reactive group (Roche's position), or whether the term should be defined without regard to how those reactive groups are used (Enzo's position).[1] Roche's construction is supported by the plain meaning of the term and the intrinsic evidence generally.

The term "***reactive*** group" inherently describes the property of having the ability to react. A person of ordinary skill in the art ("POSA") reading the patent specification and file history would understand that the reactive groups recited in claim 1 were chosen ***because*** of how they are used in reactions, and because they are the groups found on the types of molecules defined by A[3]. *See* Leighton Reply Decl. ¶¶ 6-7.[2] Enzo itself acknowledges that the reactive group (a) undergoes a reaction; and (b) bonds with an –X- moiety to form the detectable molecule. *See* Enzo Br. at 10; Sherman Decl. ¶¶ 22-24; Leighton Reply Decl. ¶¶ 8-9. This is consistent with Enzo's statement during prosecution that "[t]he purpose of this reactive group is to bond with an -X- moiety to form the Det[b] labeled compound of the invention." Exhibit 12 to Leighton Op. Decl., 9/13/89 Response to Office Action at 8; *see also* Roche Op. Br. at 7. Enzo's proposed construction of "residue comprising an activated carbon," one of the reactive groups recited in claim 1, is also instructive because Enzo agrees that the carbon atom must be "capable of forming a bond with X." Enzo Br. at 12. Taken together, the claim language, intrinsic evidence, and Enzo's admissions, support adoption of Roche's proposed construction.

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[1] Appendix A to this brief shows the parties' proposed constructions of each disputed claim term of the '523 Patent.

[2] Roche submits the Declaration of Professor James L. Leighton, Ph.D. in Support of Plaintiff Roche's Responsive Claim Construction Brief Regarding U.S. Patent No. 4,943,523, dated January 24, 2014 [hereinafter "Leighton Reply Decl."]. Dr. Leighton's Declaration in Support of Plaintiff Roche's Opening Claim Construction Brief Regarding U.S. Patent No. 4,943,523 is referred to herein as "Leighton Op. Decl."

2. "at least one modifiable reactive group" / "modified reactive groups"

Here, the key issue is whether these claim terms are, as Roche contends, indefinite. Enzo argues that a POSA would understand these terms to refer to the one or more reactive chemical groups which are modifiable and become part of A^3 so as to give a modified A^3 that can attach to X. *See* Enzo Br. at 10. To the contrary, a POSA would not know from the claim language or from Enzo's proposed construction whether the claimed (*i.e.*, final) detectable molecule must contain "at least one modifiable reactive group," as claim 1 states, or whether all of the modifiable reactive groups could have reacted to become "modified reactive groups," as recited later in claim 1. Dr. Leighton previously illustrated the difference between these two interpretations. Leighton Op. Decl. ¶ 48; *see also* Leighton Reply Decl. ¶¶ 10-11.

Even Enzo is unclear as to whether the "at least one modifiable reactive group" must become modified. In its brief, Enzo states that the one or more modifiable reactive groups "are capable of, but ***do not necessarily***, attach A^3 to the X module." Enzo Br. at 10 (emphasis added). In the very next sentence, Enzo states that the modifiable reactive group "***necessarily becomes 'modified'*** when A^3 is attached to X." *Id.* Because it is unclear how claim 1 should be interpreted—even Enzo, the patentee, does not know—it is indefinite.[3] *See Novo Indus., L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1358 (Fed. Cir. 2003).

3. "E"

Roche's construction does not seek to add a method step to the claim, as Enzo suggests. *See* Enzo Br. at 13. Rather, as explained by Dr. Leighton, the meaning of E would be understood by a POSA to include the well-known chemical properties that are common to the particular chemical groups recited, *i.e.*, O, NH, and an acyclic divalent sulfur atom. *See* Leighton Reply Decl. ¶¶ 12-13. A POSA would understand that these chemical groups are formed by a specific type of chemical reaction, called a nucleophilic reaction. *See id.* In every one of the molecules

[3] Enzo incorrectly argues that Roche's indefiniteness argument is inconsistent with its position that "reactive group" can be construed. *See* Enzo Br. at 11. The term "reactive group" is capable of construction, as discussed above; however, as used in the claims of the '523 Patent, the meanings of "at least one modifiable reactive group" and "modified reactive group," would be unclear to a POSA. *See* Leighton Reply Decl. ¶ 10.

discussed in the '523 Patent specification, the "E" element was part of a nucleophilic group that underwent a reaction to form a bond to R^1 or to Det^b, consistent with Roche's proposed construction. *See id.* ¶ 14.

As Dr. Leighton explains, a POSA would understand the synthesis of the claimed detectable molecule to be an essential feature in understanding the claim elements in the context of the patent specification. *See* Leighton Reply Decl. ¶ 4. This is clear from the way in which Enzo chose to define each claim element, including E. *See id.*; Leighton Op. Decl. ¶¶ 52-53; *Andersen Corp. v. Fiber Composites*, LLC, 474 F.3d 1361, 1375 (Fed. Cir. 2007) ("[P]rocess steps can be treated as part of a product claim if the patentee has made clear that the process steps are an essential part of the claimed invention."); *see* '523 Patent, 3:24-30, 1:10-13 ("[t]he invention . . . relates to the products obtained from these methods").

4. "comprising biotin or a substituted or unsubstituted metal chelator or a compound capable of yielding a metal chelator"

Rather than imposing a reasonable limit on the scope of this claim term consistent with the intrinsic evidence, as Roche proposes, Enzo argues that a POSA would understand "comprising" to be entirely open-ended. *See* Enzo Br. at 14. Enzo cites no evidence from the '523 Patent specification or prosecution history to support its position. Instead, Enzo bases its argument entirely on the notion that the word "comprising" is open-ended, and therefore permits "Det^b" to encompass unlimited additional atoms. *See id.* However, "'[c]omprising' is not a weasel word with which to abrogate claim limitations." *Spectrum Int'l, Inc. v. Sterlite Corp.*, 164 F.3d 1372, 1380 (Fed. Cir. 1988); *see also Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1272 n.8 (Fed. Cir. 1986). Judge Sprizzo has already cautioned against "infinitely expand[ing] the scope of the claim" in this manner, when he construed "A^3–$(X–R^1–E–Det^b)_m$" in the related '440 Patent. *See* Exhibit 4 to Khan Op. Decl., July 17, 2006 Memorandum and Opinion on Claim Construction, at 16 n.19; Roche Op. Br. at 13.

Roche's proposed construction is not overly restrictive. It does not preclude additional atoms beyond those in biotin, the metal chelator, or the compound capable of yielding a metal

chelator; nor does it limit the identity, number, or arrangement of the additional atoms. *See* Leighton Reply Decl. ¶ 16. Instead, Roche's proposed construction defines the chemical nature of the additional atoms, *i.e.*, that these atoms link the specified molecules to E, consistent with the understanding that a POSA would have from the '523 Patent claims and specification. *See id.* at ¶¶ 15, 16, 19.

5. "biotin"

Roche's proposed construction for biotin is ***exactly*** what Enzo proposed in its interrogatory responses in this litigation. *See* Exhibit 8 to Khan Op. Decl., Enzo's Response to Roche's Interrogatory No. 2, dated February 22, 2005. In an effort to avoid its admission, Enzo points to language in the specification that describes various biotin "moieties," "analogs," or "derivatives." *See* Enzo Br. at 14-15. But the claims only recite "biotin," not "biotin moieties," "biotin analogs," and/or "biotin derivatives." *See, e.g.*, *TIP v. Phillips & Brooks/Gladwin*, 529 F.3d 1364, 1373 (Fed. Cir. 2008) ("Our precedent is replete with examples of subject matter that is included in the specification, but is not claimed."). That the specification also describes unclaimed chemical structures supports Roche's interpretation of the term "biotin," because Enzo could have used the broader terms to capture biotin variants but chose not to do so. *See* Leighton Reply Decl. ¶ 20. As Enzo has already admitted, a POSA would understand the term "biotin," standing alone, to be the chemical compound reflected in Roche's construction. *See* Leighton Reply Decl. ¶¶ 17-19.

6. "chelator" / "compound capable of yielding a metal chelator"

Enzo proposes the same construction for two different claim terms—"chelator" and "compound capable of yielding a chelator." *See* Enzo Br. at 15. That approach is flawed as a matter of law because different claim terms are presumed to have different meanings. *See Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1382 (Fed. Cir. 2008) ("Our precedent instructs that different claim terms are presumed to have different meanings."). It is also scientifically incorrect because a POSA would understand that a compound "***capable*** of

yielding" another compound must be modified in some way before it yields that other compound. *See* Leighton Reply Decl. ¶ 25; *see id.* ¶¶ 22-23.

Enzo's proposed construction is also flawed insofar as it would allow for a "chelator" to be "part of a chelate," meaning that, if a detectable molecule contains a chelate, it also contains a chelator. As explained in Roche's opening brief, a chelator and a chelate are two distinct compounds, with different chemical properties and structures. Roche Op. Br. at 15; *see also* Leighton Reply Decl. ¶ 21. The passages in the specification and claims cited by Enzo support Roche's proposed construction, given that they depict chemical compounds that are explicitly described as "chelators," and not "chelates." Leighton Reply Decl. ¶¶ 22-24.

With respect to the term "compound capable of yielding a chelator," Enzo ignores the statement it made during the prosecution of the parent application that "one skilled in the art would understand claim 1 to mean that when Det^b is a compound capable of yielding a metal chelator, Det^b is ***converted to*** a metal chelator as part of the detection process." Exhibit 21 to Leighton Op. Decl., 8/26/86 Response to Office Action at 4 (emphasis added); *see also* Leighton Reply Decl. ¶ 26. Enzo cannot run from the very definition of this term that it gave to the Patent Office. *See Andersen*, 474 F.3d at 1375; *Southwall Techs, Inc. v. Cardinal IG, Co.*, 54 F.3d 1570, 1576-77 (Fed. Cir. 1995).

7. "a residue comprising an activated carbon"

The key dispute here is whether this term should be defined as it is used in the specification (Roche's position), or whether it should be defined according to a supposed "plain meaning" definition that lacks any intrinsic or extrinsic support (Enzo's position). Enzo contends that this term should be accorded its "plain and intended meaning," but fails to identify any evidentiary support for its construction, "a group of atoms which includes at least one reactive carbon capable of forming a bond with X." Enzo Br. at 12.

Enzo's interpretation improperly reads out of the claim the term "residue," which has a specific meaning in biochemistry, and would not be understood by a POSA to refer to any

"group of atoms." *See* Leighton Reply Decl. ¶ 27. Enzo's construction suffers from the additional problem that it merely substitutes the term "reactive carbon" for "activated carbon." But "reactive carbon" is used in the specification in the same way as "activated carbon." *See* Leighton Op. Decl. ¶ 85. And even if there were any difference in the usage of the two terms, Enzo could have claimed "reactive carbon," but instead chose to claim "residue comprising an activated carbon." The mere disclosure of an alternative or broader embodiment "does not outweigh the language of the claim." *TIP,* 529 F.3d at 1373.

Moreover, to the extent that a POSA would have any general understanding of the term "activated carbon," he would understand it to mean "activated charcoal," which is clearly not the meaning of this term in the '523 Patent. *See* Leighton Reply Decl. ¶ 27. Although the term "activated carbon" is not explicitly defined in the '523 Patent, the context in which it is used in the specification provides clear guidance as to the intended meaning of the term. *See id.* at ¶¶ 28-29. Roche's proposed construction, "a monomer which contains an aromatic carbon atom that is capable of covalently reacting with an electrophilic compound," is consistent with every use of the term "residue comprising an activated carbon" in the '523 Patent specification. *See id.*

8. "said complex"

The key issue here is whether, as Roche contends, this term is indefinite. Enzo argues that "the only reading of this language that makes any sense" is to construe "said complex" as "said composition," such that step (b) of claim 15 would read, "separating any complex formed between the analyte and ***said composition***." *See* Enzo Br. at 18; '523 Patent, Claim 15. That argument is inconsistent with claim 2 of the '523 Patent, which recites the step of "separating any complex formed between ***said detectable molecule*** and said analyte." '523 Patent, Claim 2 (emphasis added). It is entirely unclear whether "said complex" refers to "the composition" (as Enzo contends), "the detectable molecule" (as set forth in claim 2), or to something else entirely. *See* Leighton Reply Decl. ¶ 30.

Enzo itself appears to be confused. In its brief, Enzo states that claim 15 requires "an

analyte bound in a complex with ***the detectable molecule*** would be separated from the rest of the original composition ingredients." Enzo Br. at 18; *see also* Sherman Decl. ¶ 40. Thus, Enzo is saying that the claimed step requires "separating any complex formed between said detectable molecule and said analyte" ***from*** the composition. That is different from Enzo's proposed construction—"separating any complex formed between the analyte and ***said composition***," *i.e.* separating analyte-composition complexes from the sample. *See* Enzo Br. at 18. The Court should decline Enzo's invitation to correct any error in claim 15, because it is not an "obvious minor typographical or clerical error" that is "not subject to reasonable debate." *See Novo Indus.*, 350 F.3d at 1357. There is no way for the Court (or the parties) to determine whether the "separating" step in claim 15 requires (i) "separating any complex formed between the analyte and said composition" from the sample; or (ii) "separating any complex formed between the analyte and said detectable molecule" from the composition. *See* Leighton Reply Decl. ¶¶ 31-32.

III. THE '830 PATENT

A. CONSTRUCTIONS OF DISPUTED CLAIM TERMS

1. "oligo- or polynucleotide"

The key issue here is whether the claimed "oligo- or polynucleotide" must be a probe, as Roche contends.[4] In arguing to the contrary, Enzo ignores its own repeated characterizations of the claimed invention, including in the title, specification, and prosecution history of U.S. Patent No. 5,082,830 ("the '830 Patent"). *See* Cantor Reply Decl. ¶ 5;[5] Roche Op. Br. at 20. Enzo's arguments that requiring the "oligo- or polynucleotide" to be a probe would import a specific use into the claims (Enzo Br. at 20-21) is scientifically incorrect because a "probe" further defines the structure of the claimed "oligo- or polynucleotide." Cantor Reply Decl. ¶ 5. But even if Enzo were somehow correct that a "probe" specifies an intended use, the '830 Patent's statements regarding the functionality of the claimed invention are binding. *See, e.g.*, *Verizon*

[4] Appendix B to this brief shows the parties' proposed constructions of each disputed claim term of the '830 Patent.
[5] Roche submits the Declaration of Charles R. Cantor, Ph.D. in Support of Plaintiff Roche's Responsive Claim Construction Brief Regarding U.S. Patent No. 5,082,830, dated January 24, 2014 [hereinafter "Cantor Reply Decl."]. Dr. Cantor's Declaration in Support of Plaintiff Roche's Opening Claim Construction Brief Regarding U.S. Patent No. 5,082,830 is referred to herein as "Cantor Op. Decl."

Servs. Corp. v. Vonage Holdings Corp., 503 F.3d 1295, 1308 (Fed. Cir. 2007) (finding that "the term 'localized wireless gateway system' must be limited to one performing compression and packetization functions at the gateway" because the specification describes the present invention as such). The fact that claim 18 refers to an "oligo- or polynucleotide probe," while claim 1 does not explicitly refer to the "oligo- or polynucleotide" as a probe (Enzo Br. at 21), is irrelevant given that Enzo has clearly defined the scope of the claimed invention as an oligo- or polynucleotide probe and distinguished prior art on that basis. *See* Roche Op. Br. at 20-21; Cantor Op. Decl. ¶¶ 62-64; *Marine Polymer Techs, Inc. v. HemCon, Inc.*, 672 F.3d 1350, 1359 ("[C]laim differentiation is 'not a hard and fast rule and will be overcome by a contrary construction dictated by the written description or prosecution history.' . . . Such description appears in the specification here, as indicated above").

Enzo erroneously argues that the specification describes the use of the claimed "oligo- or polynucleotide" for purposes other than as a "probe." Enzo Br. at 21. For support, Enzo cites to a passage in the specification that defines the term "analyte-specific moiety;" however, that term appears nowhere in the '830 Patent claims. *See* Cantor Reply Decl. ¶ 7. The specification, in fact, distinguishes between the broader term "[a]nalyte-specific moiety" and "DNA hybridization assay oligonucleotide probes," confirming that the claimed "oligonucleotides" are probes. *Id.*

With respect to whether the term "oligo- or polynucleotide" is limited to naturally occurring nucleotides, Enzo has not pointed to anything in the intrinsic evidence to suggest that the patentees intended to claim any modification to nucleotides other than the modification necessary to attach the nonradioactive moieties, *i.e.* labels, to the 5' and 3' end nucleotides. *See* Cantor Reply Decl. ¶ 8. Enzo points to passages in the specification that merely indicate that the inventors tested the efficacy of incorporating the label at various positions along the probe. Enzo Br. at 21. But the claims are not directed to the various probes that the inventors experimented on—they are only directed to an "oligo- or polynucleotide" with "nonradioactive moieties" at the 3' and 5' ends. Indeed, Enzo specifically disclaimed any other modifications during prosecution when it stated that "***more is not always better*** when it comes to attaching additional biotin

moieties to an oligo- or polynucleotide" and that the prior art "clearly teaches away from the instant invention, which is directed to the 5' and 3' end labeling of an oligo- or polynucleotide using non-radioactive moieties." Cantor Reply Dec. ¶ 12; Exhibit 7 to Cantor Op. Decl., Response Under 37 C.F.R. §1.115 (Oct. 25, 1990), at 21.[6]

2. "having"

The parties dispute whether the claim term "having at least one" applies only to the ***number*** of nonradioactive moieties at the 3' and 5' ends of the claimed nucleotides (Roche's position), or whether the term makes the claim generally open ended such that the claim would cover additional modifications or additional nonradioactive moieties at locations other than the 3' and 5' ends (Enzo's position). There is no merit to Enzo's position. The "at least one" clause modifies "nonradioactive moieties," which indicates that there may be one or more "nonradioactive moieties" at each end. In other words, the "at least one" clause merely specifies the open-ended nature of the ***number*** of nonradioactive moieties at each end, but does not render the entire claim open-ended.[7]

Enzo's statements during prosecution that "***more is not always better*** when it comes to attaching additional biotin moieties to an oligo- or polynucleotide" and that the prior art "teaches away from the instant invention, which is directed to 5' and 3' end labeling" support Roche's proposed construction. Exhibit 7 to Cantor Op. Decl., Response Under 37 C.F.R. §1.115 (Oct. 25, 1990), at 21. Adopting Enzo's proposed construction would be contrary to the patent's repeated statements defining the claimed invention in terms of a probe labeled at the 5' and 3'

[6] Enzo's citation to a Roche document referring to "LNA oligonucleotides" (Enzo Br. at 21-22) supports Roche's construction, not Enzo's. Consistent with the understanding of a POSA, the term "LNA oligonucleotide" refers to a modified nucleotide but the term "oligonucleotide," standing alone and without any adjective or adjective clauses, does not. Cantor Reply Decl. ¶ 9. Using the term "LNA oligonucleotide" is akin to using the terms "synthetic nucleotide" or "modified nucleotide," wherein the adjective or adjective clause indicates that the nucleotide is not naturally occurring. *Id*.

[7] *Advanced Card*, cited by Enzo (Enzo Br. at 22), is inapposite. There, the Court construed the claim term "the card having a portion thereof projecting from the card carrier" to mean "the card having *at least* a portion thereof projecting from the card carrier," relying on the specification that described the claimed invention as "having at least a portion." 410 F. Supp. 2d 158, 167 (S.D.N.Y. 2006). Based on the patent at issue there, the Court found that the claim was open-ended with respect to the ***amount*** of the projected portion, but did not find that the entire claim was open-ended insofar as it could also include other, additional unspecified elements or projected portions.

ends and also emphasizing the signal enhancement properties of that specific arrangement. Cantor Decl. ¶ 11.

Finally, Enzo misinterprets the language of claims 10 and 11 in arguing that they support an open-ended construction of "having." *See* Enzo Br. at 22-23. A POSA would understand that the "biotinylated polymer" attached to "at least one of said end nucleotides" is a specific example of the "non-radioactive moiety" recited in claim 1.[8] *See* Cantor Reply Decl. ¶ 10.

3. "at least one non-radioactive moiety . . . attached to each of the 5' and 3' end [terminal] nucleotides"

Enzo erroneously argues that Roche is seeking to reinterpret the term "nonradioactive moiety," which the Federal Circuit has construed to mean "a moiety that is utilized in indirect detection, i.e., a moiety that can be detected with a preformed detectable molecular complex." Enzo Br. at 19-20. In fact, Roche's proposed construction identifies a ***structural*** feature of the claimed "oligo- or polynucleotide" by clarifying the ***identity*** of the "at least one non-radioactive moiety." *See* Cantor Reply Decl. ¶ 12. Enhancement of signal generation is an intrinsic property of the claimed molecule, which is not a single "nonradioactive moiety" by itself, but is instead a nucleic acid probe attached to at least ***two*** nonradioactive moieties (one at each end). *See id.* The fact that the individual nonradioactive moieties have been previously construed to require that they be "utilized in indirect detection" has nothing to do with this additional claim construction position advanced here by Roche.

Enzo fails to address the clear statements in the specification and file history describing the purpose of the claimed invention in terms of enhanced signal generation. Enzo instead argues that the specification describes other features associated with the claimed invention, such as stability and non-interference. Enzo Br. at 24. But those additional features are not inconsistent with the stated purpose of the claimed invention, which is enhancement of signal generation. *See* Cantor Reply Decl. ¶¶ 12-13. The oligo- or polynucleotide probe's ability to

[8] In any event, the use of the term "having" in claim 1 stands in stark contrast to the repeated use of the term "comprising" in the other claims. Roche Op. Br. at 22. Enzo should be precluded from advancing a claim construction that it could have achieved by using the term "comprising," which it clearly knew how to do.

hybridize and form a stable complex with a target sequence are not separate inventions, but are integrated functions that achieve the "principal advantage of the claimed invention" as stated in the '830 Patent—enhanced signal generation. Cantor Reply Decl. ¶¶ 12, 14.

Enzo's argument that Roche is attempting to import functional limitations into the claims (Enzo Br. at 23-24) is also misplaced. Requiring enhanced signal generation imposes structural constraints on the claimed probe, as discussed above. Cantor Reply Decl. ¶ 12. Regardless, there is nothing improper about imposing functional limitations where, as here, the patentee has defined the invention in that manner and/or distinguished prior art on that basis. *See, e.g.*, *Verizon*, 503 F.3d at 1308. Indeed, Enzo distinguished a prior art reference—the McCormick patent—solely on the grounds that it "does not necessarily enhance signal generation and sensitivity." Cantor Reply Decl. ¶ 12. Roche's proposed construction is appropriate based on this representation alone. This, as well as all of the other intrinsic evidence cited by Roche, demonstrates that the claimed invention is directed to enhancing signal generation. *Id*. The Court should therefore preclude Enzo from asserting infringement claims against Roche's products, which are the "opposite of . . the invention in the '830 patent" insofar as the interaction between the two labels ***reduces*** the signal generating output of the probe. Roche Op. Br. at 23.

4. "5' and 3' end nucleotides"

Enzo agrees with Roche that, in the context of the '830 Patent, "end nucleotide" should be construed to mean "terminal nucleotide." Enzo Br. 24 n.12. Accordingly, the proper construction of the term "5' and 3' end nucleotides" is "the first terminal nucleotide and the last terminal nucleotide, respectively, of the oligo- or polynucleotide."

5. "5' and 3' terminal nucleotides external to a target hybridization region"

The primary dispute between the parties is whether the nucleotides to which the non-radioactive moieties are attached must be external to the target hybridization region (Roche's position), or whether only the non-radioactive moieties need be external to the target hybridization region (Enzo's position). The claim language, which is of paramount importance

to claim construction, recites "5' and 3' terminal ***nucleotides*** external to a target hybridization region." This claim language, which Enzo ignores in its brief, demonstrates that the 5' and 3' end nucleotides must be "external," *i.e*. not complementary, to a target hybridization region. *See* Cantor Reply Decl. ¶ 15. Further, the '830 Patent specification describes that the nonradioactive moieties "external" and/or "outside" the target hybridization sequence ***are in each instance attached*** to nucleotides that cannot hybridize with the target sequence. *See* '830 Patent, col. 9:37-40 ("The 5' terminal base of this oligomer cannot hybridize to the target . . . due to noncomplementarity"); Cantor Reply Decl. ¶ 16. Accordingly, in each of those examples, the nucleotide is also "external" or "outside" the target hybridization sequence. *Id*.

IV. ALL OF ROCHE'S PROPOSED CONSTRUCTIONS WERE TIMELY RAISED.

Enzo contends that several of Roche's proposed constructions are "untimely," notwithstanding the fact that ***all*** of those constructions were fully disclosed in the parties' joint claim construction statement. Enzo's argument should be rejected outright because it did not bring a timely motion to strike the relevant portions of the parties' joint claim construction statement, nor did Enzo seek to meet and confer with Roche to discuss whether the parties would be able to resolve this dispute (even partially) without judicial intervention. *See GameTek LLC v. Facebook, Inc.*, No. 12-CV-501, 2013 WL 1412195, *2 (S.D. Cal. Apr. 8, 2013) (denying motion to strike because moving party "was obligated to make a good faith effort to meet and confer to resolve this dispute before bringing the present motion" "to strike . . . new proposed construction and extrinsic evidence"). Indeed, Enzo ***refused*** Roche's repeated offers to even discuss the allegedly "untimely" constructions and/or to potentially cure or ameliorate whatever prejudice Enzo believed it may have suffered. *Cf*. Local Patent Rule 11 (parties must "cooperate"); *Elan Microelectronics Corp. v. Pixcir Microelectronics Co*., No. 2:10-CV-00014, 2013 WL 4101813, *5-*6 (D. Nev. 2013) (meet-and-confer process breaks down where "one party has acted in bad faith by . . . refusing to negotiate").

On the merits, Enzo cites no legal authority for the untenable position that Roche should be precluded from advancing certain claim constructions either because (i) Roche did not

identify the particular dispute in the very first meet-and-confer with Enzo on claim construction, though it did so ***in response*** to Enzo's positions and ***prior*** to the filing of the parties' joint claim construction statement; and/or (ii) Roche modified its initial construction of disputed terms ***in response*** to Enzo's constructions and ***prior*** to the filing of the parties' joint claim construction statement. Enzo's arguments are not only inconsistent with the letter and spirit of the Local Patent Rules and the Court's scheduling order, they are also directly contrary to patent law and practice, which readily permits (and indeed, encourages) parties to identify additional disputes and adapt their proposed constructions in response to the opposing parties' positions leading up to the filing of the joint claim construction statement. A contrary view would turn the meet-and-confer process on its head and significantly undermine the purpose a joint claim construction filing, which is to identify and refine ***all*** of the parties' claim construction disputes before trial.[9]

Both the Local Patent Rules and the Court's scheduling order were drafted with that purpose in mind. Under Local Patent Rule 11, the parties are required to "cooperate and jointly file a Joint Disputed Claim Terms Chart listing the disputed claim terms and phrases, including each party's proposed construction." In drafting the proposed scheduling order that the Court ultimately entered, Roche proposed certain milestones in advance of the filing to make sure that the parties were engaging each other on claim construction issues before approaching the Court to resolve any disputes between them. Thus, Roche proposed that the parties "shall meet and confer to determine which claim terms and phrases the Court may need to construe" (by September 20, 2013) and then "exchange a list of those claim term(s)/phrase(s) with proposed claim constructions and extrinsic evidence" (by October 4, 2013). Exhibit 1 to Khan Reply Decl., February 9, 2013 Case Management Plan and Scheduling Order, ¶ 10(a), (b).

Importantly, Roche did not propose, and the scheduling order does not state, that the parties were to exchange "***final*** claim terms and phrases" and/or the "***final*** list of those claim

[9] *See* Patent Case Management Judicial Guide at 5-7 ("[Meet-and-confer] procedures help to ensure that the issues for the *Markman* hearing be specified in advance of the briefing cycle, as opposed to having issues disclosed for the first time in briefing. Ordering a meet-and-confer process also helps to ensure that the parties' briefing is not wastefully directed to false or merely hypothetical disputes. Ordering parties to disclose their claim construction positions also discourages 'hidden' disputes that may otherwise arise at trial.")

term(s)/phrase(s) with proposed claim constructions." *See also Toro Co. v. Ingersoll-Rand Co.*, 545 F. Supp. 2d 933, 941 (D. Minn. 2008) ("The Order did not preclude a party from deviating from its initial list of disputed terms."). Nor did Enzo believe that the parties were required to exchange final lists of terms and constructions under paragraphs 10(a) and (b) of the scheduling order. In an October 25, 2013 joint letter to the Court filed ***after*** the parties exchanged their proposed constructions pursuant to paragraph 10(b), the parties requested an extension of the deadline to file their joint claim construction statement, in part, because they had identified "new issues which require further exploration/clarification." Exhibit 2 to Khan Reply Decl., October 25, 2013 Joint Letter to the Court, at 1.

Indeed, district courts routinely allow parties to propose disputed terms and/or modify constructions up to the filing of the joint claim construction statement.[10] In any event, Enzo could not have been prejudiced by any allegedly "untimely" constructions because it had ample opportunity to consider those constructions, as set forth in Roche's section of the joint claim construction statement, and to then address those constructions in its briefing (which Enzo did).[11] And, in its briefing, Enzo actually ***disputes*** the proposed constructions that were allegedly "untimely," which means that the meet-and-confer and joint claim construction process succeeded in identifying the parties' material claim construction disputes in advance of trial.[12]

V. CONCLUSION

For the foregoing reasons, the Court should adopt Roche's proposed constructions of the disputed claim terms of the '830 and '523 patents.

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[10] *See, e.g., Vita-Mix Corp. v. Basic Holdings, Inc.*, 514 F. Supp. 2d 990, 993 (N.D. Ohio 2007) (denying motion to strike allegedly "allegedly late disclosure of its claim construction contentions"); *Toro,* 545 F. Supp. 2d at 941 (addressing "disputed terms in the parties' Joint Claim Construction Statement in their entirety" over patentee's objection to the consideration of two of the terms that the accused infringer had not identified on its "pre-conference list of claim terms."); *see also Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 763 F. Supp. 2d 671, 682 n.10 (D. Del. 2010) (party did not "waive its opportunity to present its proposed construction" even where it was not included "on the list of ten terms that the Court originally allowed.").

[11] *See, e.g.*, *Vita-Mix*, 514 F. Supp. 2d at 993 ("The Court finds that plaintiff had adequate time after the meet and confer to prepare its own claim construction in its opening brief and to also address defendant's revised constructions in its rebuttal brief.").

[12] *See O2 Micro*, 521 F.3d at 1362 ("By failing to construe this term, the district court left the jury free to consider these arguments.").

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Respectfully submitted,

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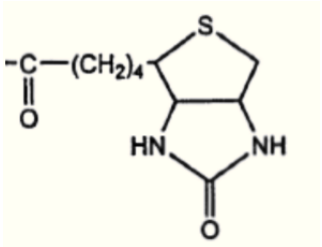
APPENDIX A – Disputed Claim Terms of the '523 Patent

Term	Roche's Proposed Construction	Enzo's Proposed Construction
"reactive group" (claim 1)	a functional chemical group that undergoes a reaction to bond with an –X- moiety to form the detectable molecule	amino, hydroxyl, 1,2-cis diOH, halide aryl, imidazoyl, carbonyl, carboxyl, thiol or a residue comprising an activated carbon
"modifiable / modified reactive group" (claim 1)	The terms "at least one modifiable reactive group" and "modified reactive groups" are indefinite under 35 U.S.C. § 112, 2nd paragraph.	The terms "at least one modifiable reactive group" and "modified reactive groups" are both definite and readily understood to refer to the one or more reactive chemical groups which are modifiable and become part of A^3 so as to give a modified A^3 that can attach to X.
"E" (claim 1)	O, NH or an acyclic divalent sulfur atom, which underwent a reaction to form a bond to R^1 or to Det^b	O, NH or an acyclic divalent sulfur atom
"comprising biotin or a . . . metal chelator or a compound capable of yielding a metal chelator" (claim 1)	biotin, a substituted or unsubstituted metal chelator or a compound capable of yielding a metal chelator, plus any atoms used to link the biotin, substituted or unsubstituted metal chelator or compound capable of yielding a metal chelator to E	The term "comprising" is open-ended and allows for atoms in addition to those specified.
"biotin" (claims 1, 15, 20, and 40)		any biotin moieties, derivatives, or analogues which may be used wherever biotin/avidin or biotin/streptavidin-based pairs or detection systems have been used in the prior art
"chelator" (claims 1, 15, and 40)	a chemical compound that can form coordinate bonds with a metal ion to form a complex called a chelate	a chemical compound/agent which can complex or combine with a metal ion to become part of a chelate

Term	Roche's Proposed Construction	Enzo's Proposed Construction
"compound capable of yielding a metal chelator" (claim 1)	a compound that is converted to a metal chelator as part of the detection process	Enzo's position is that any construction of this term should not include the language "converted … as part of the detection process."
"residue comprising an activated carbon" (claim 1)	a monomer which contains an aromatic carbon atom that is capable of covalently reacting with an electrophilic compound	a group of atoms which includes at least one reactive carbon atom capable of forming a bond with X
"said complex" (claim 15)	The term "said complex" is indefinite under 35 U.S.C. § 112, 2nd paragraph.	This claim phrase is both definite and readily understood to refer to the composition which is said to bind, or complex, with the analyte.

APPENDIX B – Disputed Claim Terms of the '830 Patent

Term	Roche's Proposed Construction	Enzo's Proposed Construction
"oligo- or polynucleotide" (claims 1 and 12)	a nucleic acid probe in which the nucleotides, other than those at the 5' and 3' ends, are naturally-occurring	a chain of three or more nucleotides directly linked to each other in an uninterrupted continuous sequence
"having" (claims 1 and 12)	consisting of, *i.e.*, excluding any element not specified in the claim	This term allows for elements in addition to those specified in the claim.
"at least one non-radioactive moiety…attached to each of the 5' and 3' end nucleotides" (claim 1) / **"terminal nucleotides"** (claim 12)	at least one non-radioactive moiety . . . attached to each of the 5' and 3' end nucleotides, to enhance the signal generating output of the oligo- or polynucleotide	Plain meaning
"5' and 3' terminal nucleotides external to a target hybridization region" (claim 12)	The 5' and 3' terminal nucleotides are external, i.e., not complementary, to a target nucleic acid sequence.	The non-radioactive moieties must be external to a target hybridization region, but the 5' and 3' terminal nucleotides can be within the target hybridization region.